UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/937,756	09/25/97	RUEGER	D CRP-070FWCN2

HM22/0925

IVOR R. ELRIFI
MINTZ LEVIN
ONE FINANCIAL CENTER
BOSTON MA 02111

EXAMINER	
TURNER, S	
ART UNIT	**PAPER NUMBER**
1647	18

DATE MAILED: 09/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/937,756	Applicant(s) Rueger et al.
	Examiner Sharon L. Turner, Ph.D.	Group Art Unit 1647

☒ Responsive to communication(s) filed on 7-6-00

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 88, 90, 91, 97, 99, 105, and 106 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 88, 90, 91, 97, 99, 105, and 106 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Response to Amendment

1. The Examiner of U.S. Patent application SN 08/937,756 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1647.

Continued Prosecution Application

2. The request filed on 7-6-00 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/937,756 is acceptable and a CPA has been established. An action on the CPA follows.

3. The amendment filed 7-6-00 has been entered into the record and has been fully considered.

4. Claims 83, 85, 89, 92, 95, 98 and 101 are canceled. Claims 88, 90-91, 97, 99, 105 and 106 are pending.

5. As a result of applicants amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Rejections Maintained

Double Patenting

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 97 and 99 stand provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 7 and 9 of copending Application No. 08937,755. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Applicants request that the rejections be held in abeyance pending a determination of otherwise allowable claims in the pending application.

Applicant's arguments filed 7-6-00 have been fully considered but they are not persuasive. Rejections can not be held in abeyance until indication of allowable subject matter. Applicant is required to amend the claims such that the subject matter is not the same in order to overcome the rejection of record.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 90-91 and 105-106 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-7 and 9 of copending Application No. 08/937,755. Although the conflicting claims are not identical, they are not patentably distinct because the species recited anticipate the genus claims in the '756 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request that the rejections be held in abeyance pending a determination of otherwise allowable claims in the pending application.

Applicant's arguments filed 7-6-00 have been fully considered but they are not persuasive. Rejections can not be held in abeyance until indication of allowable subject matter. Applicant is required to amend the claims such that the subject matter is not overlapping in order to overcome the rejection of record.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 88, 90-91 and 105-106 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants argue that the rejection is "without observance of procedure required by law" Administrative Procedures Act 5 USC § 706(2)(D). Applicants allege that p. 39, line 33 to p. 40, line 1, p. 46, lines 6-12, p. 53, lines 11-25, p. 40, lines 20-34, p. 53, lines 26-35, p. 33, line 16 to p. 39, line 18, p. 76, line 1 to p. 80, line 17, Example 6 provide for adequate written description.

Applicant's arguments filed 7-6-00 have been fully considered but they are not persuasive for the same reasons of record as set forth in Paper No. 12, filed 1-6-00. Applicants are reminded that written description is required for the claimed invention. Applicants specification at p. 39, line 33 to p. 40, line 1, p. 46, lines 6-12, p. 53, lines 11-25, p. 40, lines 20-34, p. 53, lines 26-35, p. 33, line 16 to p. 39, line 18, p. 76, line 1 to p. 80, line 17, and Example 6 are insufficient to provide adequate written description for the claimed invention in particular for restoring motor function in a mammal with either spinal cord injury or amyotrophic lateral sclerosis with the recited morphogens. The passages pointed to by applicant for support merely provide cursory guidance to the encompassed sequences by reference to sequences which share percent homology, similarity, are allelic or species variants, which contain conserved skeleton domains and are functional equivalents. Such recitations in the specification do not provide adequate written description for the contemplation of restoring motor function with said morphogens in either spinal cord injury or amyotrophic lateral sclerosis. Thus the claimed invention lacks written description support.

12. Claims 88, 90-91, 97, 99 and 105-106 stand rejected under 35 U.S.C. 112, first paragraph, for the reasons made of record in Paper No. 12, mailed 1-6-00. The specification, while enabling for claims limited to methods of using OP-1 of claimed SEQ ID NO:2 to induce N-CAM and L1 expression in NG-108 cells in vitro, does not reasonably provide enablement for "treating/preserving motor function/restoring motor function" in a mammal afflicted with ALS/spinal cord injury, or for using structurally uncharacterized morphogens or biologically functional equivalents thereof to accomplish such. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants argue that the claims do not recite a method of inducing N-CAM expression in NG-108 cells and that the stimulation of N-CAM or L1 isoform production by an NG108-15 cell in vitro is a functional limitation on the morphogen and not a step in the claimed methods.

These arguments have been fully considered but are not persuasive. The examiner agrees that the stimulation of N-CAM or L1 isoform production by an NG108-15 cell in vitro is a functional limitation on the morphogen and not a step in the claimed methods. The statement in the preamble of the rejection should not be construed to the interpretation that the examiner has misinterpreted the claim. The statement of the preamble merely provides the scope of what applicant has shown enablement for.

Applicant further argue that the specification discloses methods compositions and devices for stimulating cellular repair of damaged neurons and neural pathways, including regenerating

damaged dendrites or axons and points to the specification, examples 8, and 15-18 as providing support for such enablement and concludes that these teachings and working examples clearly enable the skilled artisan to practice the claimed methods without undue experimentation.

These arguments have been fully considered but are not persuasive. First, applicants claims are drawn to methods of restoring motor function in amyotrophic lateral sclerosis, spinal cord injury, wherein such injury results from a tumor or from a chemical trauma . The examiner points to evidence in the specification which raises the issue of a lack of enablement with respect to the claims, specifically the examiner points to evidence that axonal growth in the absence of OP-1 is no better than axonal growth in the presence of OP-1. In addition, no enabling support is found for the recitations of preserving or restoring motor function in a mammal with amyotrophic lateral sclerosis, spinal cord injury or from such spinal cord injury resulting from chemical trauma or a tumor. Applicant urges that this conclusion is statistically unfeasible, yet no statistics have been provided from which the examiner can determine if such allegation is true. The example does not provide for the number of animals tested in each group and the length of axonal outgrowth in each group.

Applicant argues additionally that the examiner misreads the specification regarding the state of the art at the time of filing and that the examiner misreads the state of the art in making the enablement rejection. These arguments have been fully considered and are not persuasive for reasons of record in Paper No. 12, mailed 5-13-99. The examiner contends that all references as set forth in the enablement rejection provide valid support for a lack of enablement

commensurate in scope of the claims and provide a review of the state of the art. The following provide such evidence contrary to applicants assertions otherwise. Lein et al., Neuron, 15:597-605, 1995 teach that in the absence of NGF, few neurons survived and this number was not significantly increased in the presence of OP-1, p. 601, col. 1, last paragraph, lines 8-10. With regard to Varley et al, 203:434-37, Dev. Dynamics, 1995, adrenergic cell number is not irrelevant to the state of the art with respect to the claims as it can for example provide a measurement for cell survival. With regard to Wilson et al, 376:331-33, Nature, 1995, Wilson is not irrelevant to the state of the art for which it is being used, for example it provides an instance in which BMP-4 has been shown to function as a neural inhibitor. With respect to Withers et al, Soc. For Neurosci. Abstr., 1996, synapsin positive aggregates does not show functional synapse formation. With regard to Jackowski, 9:303-17, Brit. J. Neurosurg., 1995, Jackowski presents a review of the research upon the inability of the CNS in man to successfully regenerate following injury, and teaches that we have gained a far greater understanding of the molecular biology, pathology and other factors that lead to the adult CNS being non-supportive and indeed actively inhibitory to axonal regrowth, in particular abstract lines 1-6. If applicant wishes to show evidence to the contrary using alternative references this should be done by providing the alternative references and support by page and line number for a different conclusion of the state of the art. Jackowski is considered to be representative of the state of the art. With regard to the issue of connections on dead cells, this observation is not irrelevant to the enablement of the pending claims since the claimed treatment for and restoration of neurons of spinal cord injury

and amyotrophic lateral sclerosis must provide some way of coping or compensating for the dead and dying cells affected in the disease. Thus, connections and synapses of dead or dying neuronal cells is relevant with respect to a discussion of the enablement of such claims. NG108-15 cells are not moot with respect to a discussion of the fact that these cells do not represent in vivo neural tissue. Neurite outgrowth is not commensurate in scope with formation of connections between neurons to restore motor function and thus contrary to applicants assertion the claims are not commensurate in scope with that disclosed in the specification for treating ALS or spinal cord injury. Thus a review of the prior art as presented by the examiner in Paper No. 12 indicates the state of the art and also indicates that one of skill in the art could not have used the compound morphogen for the treatment or restoration of motor function in ALS and spinal cord injury. The specification does not teach with evidentiary support that administration of any morphogen results in the treatment or restoration as is specifically claimed. In view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 90-91 and 105-106 stand rejected under 35 U.S.C. 102(b) as being anticipated by The Regents of the University of California/Harland et al. (WO 95/06656; reference #B5 cited by applicants on PTO-1449) for the reasons made of record in Paper No. 12, mailed 1-6-00.

Applicant argues that the examiner has not set forth what specifically lacks support in the parent, that Harland's description is not enabling, and that both the rejection an the accorded filing date are logically inconsistent and unfair.

This argument is not persuasive as set forth in Paper No. 12. There is no written description in the parent application for instant claims to a method of treating ALS and spinal cord injury and to a method of preserving or restoring motor function in a mammal suffering from ALS and spinal cord injury, in particular to the homologous morphogen dor3 which is the subject of WO95/06656. As pointed out by applicants, Harland teaches the restoration of neural pathways and the alleviation of neurodegenerative diseases with a morphogens homologous to the claimed sequences. Thus, the denial of the priority date based on a lack of written description for the claims is appropriate and the rejection of record is maintained for the reasons of record.

Status of Claims

13. No claims are allowed.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
September 20, 2000

Patricia A. Duffy

PATRICIA A. DUFFY
PRIMARY EXAMINER